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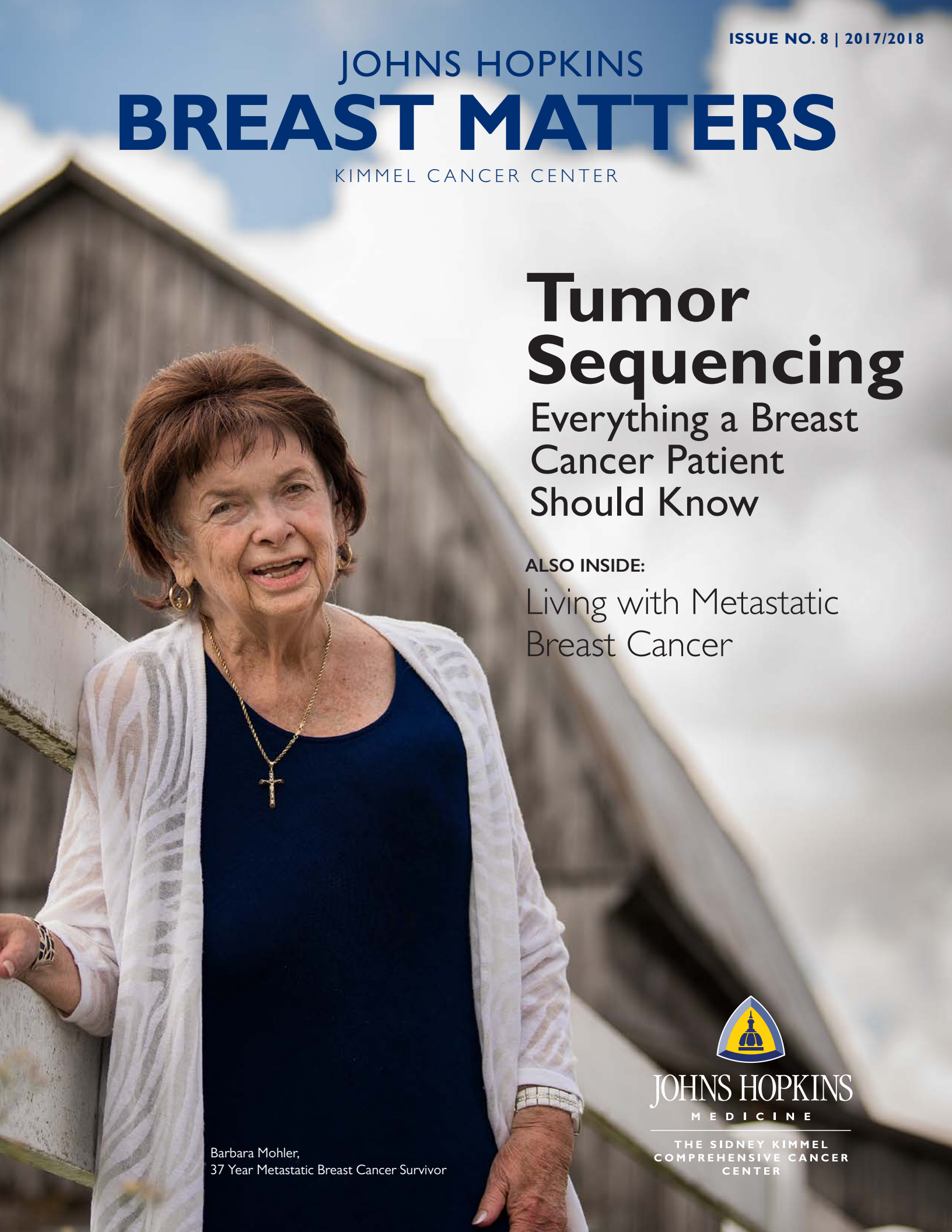
JOHNS HOPKINS

BREAST MATTERS

KIMMEL CANCER CENTER



Tumor Sequencing

Everything a Breast Cancer Patient Should Know

ALSO INSIDE:

Living with Metastatic Breast Cancer

Barbara Mohler,
37 Year Metastatic Breast Cancer Survivor

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MEDICINE

THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER

The GAITWAY Tumor Board

Everything a Breast Cancer Patient Should Know About Tumor Sequencing

With current technology, it is relatively cheap and easy to sequence the DNA of just about anyone or anything. The technology, which first gained acclaim in academic research institutions, has been used to decipher the mistakes and changes in DNA that drive cancer, and has led to dozens of companies that offer sequencing directly to patients.

Despite the ease, the ability to interpret sequencing results is still comparatively new science. Terms like genome, exome, germline and somatic are not entirely familiar to all doctors, let alone patients. The ability to decipher the data gene sequencing produces to determine what are important to the care of cancer patients are a complex science all its own.

If a shopper went to a large department store and asked for a pink dress, she might be presented with hundreds of dresses, but most of them would likely be the wrong size, style or perhaps even an undesirable shade of pink for the shopper. She would need to sort through them and pick out only the ones that suit her, and perhaps she would not find any that she liked.

Oversimplified, yes, but this scenario illustrates the problem with the broad use of gene sequencing. The technology is limited by the reader's ability to sort through it and pull out data points that will make a difference in patient care. Gene sequencing of a tumor may reveal many alterations to the DNA, but it takes an expert understanding of cancer genetics to know if any of those alterations influence a patient's cancer.

"Tumor sequencing makes a lot of information available, but how do we use it?" says sequencing and cancer genetics expert **Josh Lauring**. "Many doctors are not up to speed on the science and how the genetics impact the tumor and targeted therapies, and how they all interact. It's complex."

The clinical usefulness of alterations is also limited by currently available drugs. Identifying a genetic mistake that helps a cancer grow or spread is important to cancer research, but without a drug that can target the mistake, it has no affect on the current standard of care. By the same token, a mutation in a known cancer gene with an associated drug may not necessarily be driving the growth of the cancer. Using the drug to target this passenger mutation—the term given to gene mutations that are just along for the ride but are not actually influencing the behavior of the cancer—does nothing to abate the cancer and can actually be harmful.

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>
> **– JOSH LAURING**

Leading breast cancer genetics expert **Ben Park** witnessed this firsthand when a young breast cancer patient opted to forgo standard therapy with a proven track record of success to enroll in a clinical trial at another hospital solely based on one of these company-produced gene sequencing reports. Park, a member of the world-renowned team that became the first to decipher the genetic blueprint of breast and other cancers, discovered true cancer-promoting mutations in the gene that was identified in the report and recognized that the type of mutation that the patient had was not driving her cancer. "This clinical trial was not going to help her, but there were a half-dozen standard therapies we knew were likely to work against her cancer," Park says.

This patient nearly died as a result of an ill-advised interpretation of her sequenced tumor. "That case really showed me the danger of patients and oncologists acting on these reports without having the full knowledge to really evaluate all of the information." says Park. "Patients were chasing invalidated targets, and I recognized we needed a molecular tumor board to vet these sequencing reports."

In 2013, soon after Park shared this patient's experience with Kimmel Cancer Center colleagues, the GAITWAY Tumor Board was born. GAITWAY stands for Genetic Alteration In Tumors With Actionable Yields. Park ran GAITWAY until 2015, when he turned the reins over to Lauring. Lauring leads a board made up of about a dozen experts, including oncologists, genetics experts, molecular pathologists, genetic counselors and a patient advocate. They meet weekly to review cancer gene sequencing reports to determine if they contain any actionable targets—gene alterations that have corresponding drugs that work against them.

Lauring receives sequencing reports from other Johns Hopkins colleagues, community physicians, and Johns Hopkins partners and affiliates, such as the Allegheny Health Network and Johns Hopkins Singapore, and takes them before the GAITWAY board for review and interpretation. He is among an elite group of clinicians charged with staying

abreast of the ever-changing list of cancer gene targets and targeted therapies—drugs that target specific gene alterations. Under his leadership, GAITWAY findings have been published in scientific journals, and it has become a national model for how to navigate modern gene sequencing technology and integrate it into precision cancer medicine—the term for therapies that are based on the unique molecular characteristics of each patient's cancer.

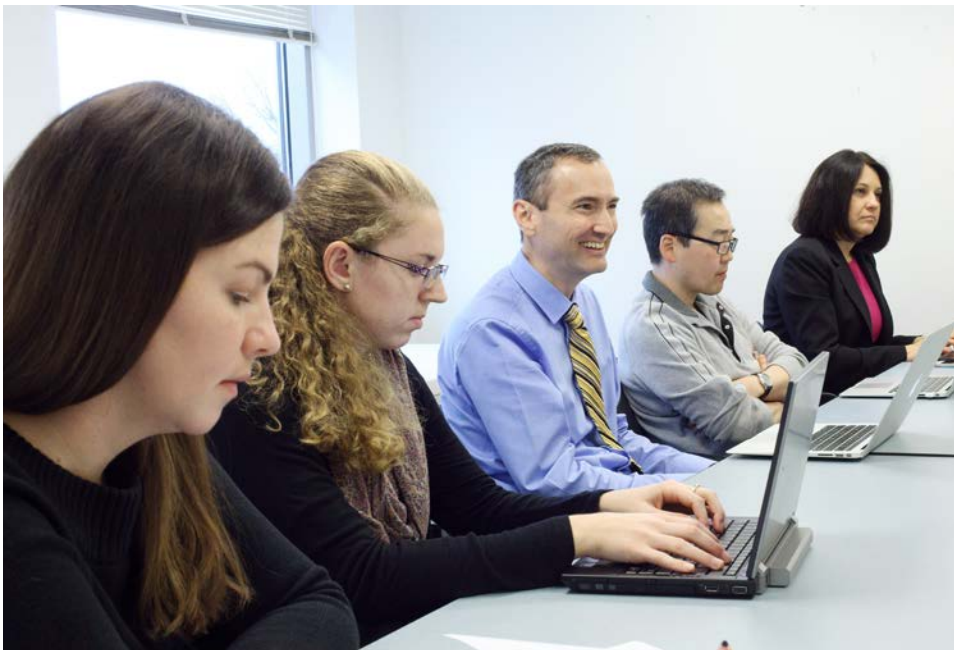
"Others can do this, but not everyone does it well," says Breast and Ovarian Cancer Program Co-Director **Vered Stearns.** "Our GAITWAY board finds things others miss."

They bring some clarity to a not-so-well-understood technology. Lauring has reviewed reports that identify a gene target, only to find that the mutation is not even in the tumor. On another occasion, GAITWAY expertise led to a completely different diagnosis for a patient—an observation that changed the treatment.

A report on a lung cancer patient came before the GAITWAY board, and Lauring recognized a gene rearrangement identified in the sequencing report occurred in a type of cancer called NUT midline carcinoma. It is a rare cancer, occurring in the trachea and chest, that many doctors have never heard of. Most of the time, the cancer is mistaken for and treated like squamous cell lung cancer. Lung cancer drugs do not work against this aggressive cancer, so Lauring's depth of expertise in cancer genetics was critical to guiding this patient to the best treatment. Because Lauring was able to tie the genetic alteration to the rare and aggressive cancer, the GAITWAY board could guide this patient to a clinical trial of emerging targeted therapies for this cancer type.

"Our goal is to get patients to the best therapy for them," says Lauring. "The expertise the GAITWAY board brings to the table is particularly important in the case of rare cancers and new or rare mutations."

In another case, Lauring and board were reviewing a prostate cancer case. The report listed the patient as MSI-negative. The term refers to a Kimmel Cancer Center discovery that uses mutations in genes termed mismatch repair to identify patients likely to respond to immunotherapy. Patients with mismatch repair alterations typically have many mutations in their tumors, and the GAITWAY board noted that this patient's tumor had that telltale sign and ordered additional pathology on the tumor. The additional testing revealed the cancer was actually MSI-positive, making the patient eligible for an immunotherapy clinical trial.



From left, Dana Petry, Jennifer Ensminger, Josh Lauring, M.D., Ph.D., Ben Park, M.D., Ph.D., and Vered Stearns, M.D.

"No test is perfect, and each company has issues with what it misses or doesn't include in its reports," says Lauring. The GAITWAY board does not simply take the reports on their face value but instead uses its broad expertise to flag and explore inconsistencies that might change treatment recommendations or provide more options to patients.

"Our job is to figure out if there is a gene in a report that we know we can target effectively with an available, FDA-approved drug now or through an open clinical trial," says Lauring. Genetic counselors on the GAITWAY board, led by **Dana Petry**, help determine when genetic counseling or additional testing for inherited gene mutations should be recommended, and the patient advocate serves as a voice for all cancer patients.

As important as finding genes that can be targeted with therapy is being able to determine that a report contains no actionable targets, Lauring says. "If the evidence is weak, we need to be able to say that too."

The GAITWAY board has reviewed 300 cases since forming in 2013. One hundred of the cases were brought to the board in 2017, demonstrating the growth in demand for the group's specialized expertise. Still, Lauring knows they can't review every case, but they are trying to be proactive working with companies to alert them to common mistakes and specific actionable targets they should look for and seek expert guidance.

What does this mean for breast cancer patients?

Stearns recognized that breast cancer patients wanted tumor sequencing, and it is her goal to learn how it can help patients now but also to advance the science to see how they can increase its benefit in the future.

The wide availability but often uncertain utility of cancer gene sequencing is particularly relevant to breast cancer experts and patients. Genes that drive cancer are not specific to a certain cancer type but often occur across cancers with varied frequency. Some cancers, such as lung cancer, have more known actionable targets. Breast cancer, while out in front in terms of precision medicine, with bio-

markers like HER2 and estrogen receptor status long guiding therapy, has very few gene mutations associated with targeted treatments.

"One thing cancer genetics has taught us is that no two cancers are alike," says Lauring. "Breast cancer does not yet have many actionable genetic targets, but it has so many approved standard treatments. A patient could go through 10 treatments before we would start to worry about running out of options and would recommend sequencing a tumor to see if it will point to something that directs us to a clinical trial." That scenario may come up sooner for patients with triple-negative breast cancer, or other cancers, like pancreatic cancer, where there are fewer treatment options. "Right now, the main utility is for women with recurrent, metastatic breast cancer," he says.

Lauring and Park say there is really no reason for an early-stage, surgically treatable cancer to be sequenced. "There are so many good standard therapies. We don't want to mess around with curable disease," says Park. "But, in metastatic patients whose cancers continue to grow on standard therapies, we know another chemotherapy is not going to make a difference. These are the patients we need to sequence and look for molecular targets."

With many companies selling this service and using different platforms to sequence genes in cancers, it is a little bit like the Wild West now. Research is leading to more and more drugs being studied and approved for genetic alterations. One day, this may be routine cancer medicine, but currently there are more questions than answers. As a result, where and how the test is reviewed absolutely make a difference. The GAITWAY Tumor Board helps ensure that the excitement over the promise of sequencing technology does not overshadow the reality of what it can currently deliver.

Park points out that Kimmel Cancer Center experts are in a unique position to traverse this uncharted territory, as its experts were the first to map the genetic causes of cancers and are the undisputed leaders in this area of research. "The thing that bothered me the most was that too many doctors were ordering genetic testing at the wrong time," says Park. "If you have a treatment you know is going to work, why order the testing? Timing is important. Who evaluates the report is too."

"I'm not discouraging these tests, but it's important for patients to have realistic expectations and make sure to get the recommendation of knowledgeable experts," says Lauring. "This is complex stuff."

Josh Lauring, M.D., Ph.D., front, and Brian Dalton, M.D., Ph.D.

Currently, breast cancer has just a few known actionable mutations that could be identified through sequencing, Lauring says.

When an advanced breast cancer comes before the board, HER2 mutations are among the gene mutations the GAITWAY board looks for. HER2 mutations are different from the much more common HER2 amplification, a breast cancer biomarker that can be obtained without gene sequencing and is important to guiding doctors to standard therapies. "In HER2 amplification, the gene gets duplicated again and again, and this leads to a lot of HER2 protein," says Lauring. Drugs like trastuzumab, familiar to most patients by its trade name Herceptin, work well against cancers with HER2 amplification, known as HER2-positive breast cancers.

Now, however, there is evidence that certain patients with lobular breast cancer or triple-negative breast cancer, a HER2-negative and treatment-resistant form of breast cancer, may also benefit from treatment with trastuzumab. Patients whose cancers have mutations—not amplification—of the HER2 gene might see a response to the drug. "We don't know for certain yet if they will all benefit from HER2 therapies, but there are data that suggest that some of them will," says Lauring. For a triple-negative breast cancer patient with a HER2 mutation who is not benefiting from standard treatments, the GAITWAY board could suggest a clinical trial that is studying the benefit of trastuzumab in triple-negative breast cancer and variety of other cancers with HER2 mutations. Breast cancer clinical researcher **Roisin Connolly** is leading these trials at the Kimmel Cancer Center.

HER2 mutations are rare, occurring in only about 2 percent of breast cancers, compared to HER2 amplifications, which occur in about 20 percent of breast cancers. However, in certain types of breast cancer, such as lobular and triple negative, Lauring says they may be at play in about 5 to 10 percent of cases.

In women with BRCA gene mutations, drugs known as PARP inhibitors may be able to prevent cancer cells from repairing damage caused by chemotherapy and improve the effectiveness of standard treatments. This was the case for Pam Fitzgerald, a metastatic metaplastic breast cancer patient of Park's. (See article on page 6.) She was not a candidate for a clinical trial of PARP inhibitors, so the GAITWAY board recommended off-label use of the drug, and it helped keep Fitzgerald's rapidly growing cancer in check for more than a year. Recently, her cancer has begun to grow again, and Park ordered new tumor sequencing to see if the cancer has acquired any new mutations that could be targeted with a drug.

Some gene mutations, known as acquired-resistance mutations, result from chemotherapy and targeted therapies as cancer cells exploit new cellular

mechanisms to maintain their survival. Tumors that were once hormone receptor positive may shift to hormone negative. Sequencing can help identify these changes in patients with advanced cancers that stop responding to treatment. Right now, Lauring says, there are only a few new drugs that may work in patients with certain resistance mutations, but just as important, sequencing can inform doctors about therapies that are unlikely to work. For example, if a tumor has acquired a resistance mutation in the estrogen receptor, an aromatase inhibitor, which reduces the amount of estrogen available to tumors, is not likely to help. "Sequencing advancing breast cancers can help us select the right drug or avoid using the wrong one," says Lauring.

PIK3CA mutations, discovered in breast cancers in high frequency by Park in 2004, occur in about 40 percent of breast cancers. Lauring says there is early evidence that patients who have this mutation and are not responding to standard therapies may benefit from investigational drugs that block PIK3CA. "If we confirm this finding in ongoing clinical trials, we'll have a reason to test for this mutation, and it could change the landscape for breast cancer," he says.

Emerging immunotherapies are also showing promise for breast cancer, and triple-negative breast cancer in particular, which usually has a larger number of mutations and, even in the absence of mismatch repair mutations, may still attract an immune response simply because of the sheer volume of mutations. "It's still early, but this is something we can identify with tumor sequencing," says Lauring. "We're not there yet, but as immunotherapy evolves and as we understand more about targets, we may evaluate how mutations effect driver genes in the tumor, but also how they could alter the proteins in a way that might make the immune system recognize the cancer. Then we could begin to think about personalized vaccines and other types of immunotherapy."

Ultimately, Park says, he wants women to be driven by knowledge and not by fear. "I see the devastation this disease causes, and we all want women to have more options," he says. "Cancer figures out ways to get around almost everything when it becomes metastatic, and that's where having a foot in both fields—clinical care and genetics—has helped me direct laboratory research so that we can use tumor sequencing to help even more breast cancer patients in the future."

How does research help?

Lauring says there are two very important aspects of research. "There is the kind of research we do in the laboratory to help us better understand the biology of breast cancer, and then there is the human experiment all around us where patients are desperate and are requesting these tests," he says. Lauring believes there is a lot to learn from both. In addition to offering the expert advice of the GAITWAY board, they are building a database that marries tumor genetics with clinical outcomes, so they can learn more about targeted therapies that work, for whom they work best and also ones that don't work. "Genetics tell you drivers and potential targets, but there is a lot more we can learn by combining it with the patient data," says Lauring.

Through the GAITWAY program, they are collecting and analyzing information, including age, family history, genetic profile, diagnosis, stage of the cancer, treatments, length of response to treatments, recurrences and survival, to begin to draw conclusions. "It's amazing how little data we have of this kind," says Lauring. "Details about treatments received and how patients did on them do not exist." For example, they will begin to look at how many breast cancer patients had PIK3CA mutations and how they did on a specific targeted therapy compared to patients who did not receive a targeted therapy.

The group is also collaborating on research beyond the Kimmel Cancer Center, including the National Cancer Institute's MATCH trial and the American Society of Clinical Oncology's TAPUR trial. MATCH stands for Molecular Analysis for Therapy of Choice and will do what GAITWAY already does, but on a larger scale, sequencing thousands of cancer patients to look specifically for changes in 143 genes to match them to specific targeted therapies. TAPUR, Targeted Agent and Profiling Utilization Registry, is ASCO's first clinical trial and will collect data on the activity of about 10 drugs targeting specific genetic mutations across a variety of cancer types. "We're collecting real-world data with community oncologists around the country to see if tumor sequencing is helping patients and if the therapies it points to are helping patients," says Lauring.

At the Kimmel Cancer Center, Park and Stearns are conducting research studies to better determine if gene sequencing using noninvasive liquid biopsy samples works as well as, or potentially even better than, sequencing tumor samples. Two Avon Center of Excellence-funded research studies known as IMAGE, for Individualized Molecular Analyses Guide Efforts, compare both methods of using genetic information to help guide breast cancer therapy and to track and monitor the progress of cancer to see if a treatment is working.

The first IMAGE study compared tissue DNA to liquid biopsy DNA in 20 patients with triple-negative breast cancer. They wanted to see if liquid biopsy provided a more complete genetic profile of metastatic cancers than tissue biopsy, which is typically limited to sampling one metastatic site. Liquid biopsy, which gathers cancer DNA from plasma circulating throughout the bloodstream, has the potential to collect tumor DNA from all metastatic sites.

GENETICS TELL YOU DRIVERS AND POTENTIAL TARGETS, BUT **THERE IS A LOT MORE** WE CAN LEARN BY COMBINING IT WITH THE PATIENT DATA. **– JOSH LAURING**

"The results demonstrated that liquid biopsy is a good representation of tissue," says Stearns. In most of the patients, they found the same mutations in blood as in tissue, but there were six patients where they could not get adequate amounts of tumor tissue to biopsy. "Liquid biopsy provides another way to obtain tumor DNA from these patients. It provides faster results, and since it is noninvasive, we can perform the test repeatedly and potentially even replace the need for tissue biopsy," says Stearns.

The second study builds on these findings and expands the study to 200 patients and all breast cancer types. "We will be looking at tumor profiling and liquid biopsy, trying to identify targets and really understand the interplay of mutations and response to treatment," says Stearns. They will perform a liquid biopsy on all patients and tissue biopsies when possible. They will bring the genetic profile obtained from both to the GAITWAY board, which will provide each patient and her physician with therapy recommendations based on the genomic profile in tumor and blood. They will also compare liquid biopsies taken before and after treatment to look for changes in cancer DNA.

"Right now, we have to wait three months and do an imaging scan to see if a drug is working," says Stearns. "We want

to see if we can do a liquid biopsy after a week and tell if a therapy is working. If not, we can quickly switch course. We would rather know sooner than later. We don't want to lose three months."

In patients with early-stage breast cancer, Park says, about 30 percent of patients who receive chemotherapy before surgery will have no visible tumor left at the time of surgery. He, Stearns and breast cancer colleague **Antonio Wolff** would also like to see if liquid biopsy can drill down to the molecular level to identify patients who need no additional treatment from those who may have genetic evidence of remaining cancer cells. "Maybe some patients will not need surgery," says Park. They would compare liquid biopsy results before and after the course of chemotherapy given leading up to surgery. If they are able to detect cancer DNA through liquid biopsy before chemotherapy is started but find no visible tumor and no cancer DNA after the course of chemotherapy ends, perhaps these patients can avoid surgery.

"WE WOULD RATHER KNOW SOONER THAN LATER. **WE DON'T WANT TO LOSE THREE MONTHS**."
–VERED STEARNS

"It would enable physicians to identify the patients who are cancer-free—and who may not need surgery after chemotherapy or chemotherapy after surgery," says Park. "That's the biggest unmet need in breast cancer care right now. About 30 of every 100 postsurgical breast cancer patients are at a high risk for relapse and need chemotherapy, but we can't distinguish them from the patients who are cured, so we give postsurgical chemotherapy to all 100 of those patients because we can't tell. If liquid biopsy is able to identify the high-risk cases in advance, many women could be spared chemotherapy."

"All of this work looks really promising," Park says, "and it fits in nicely with our goals of precision or individualized medicine. What we're trying to do is get to a point where we can say, 'You don't need to get everything and the kitchen sink. You just need to get what your individual cancer needs so that it's cured—not too little, not too much.'" ■

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Look for Breast Matters

Pam Fitzgerald: Exemplifying the Brave New Reality of Metastatic Cancer Patients

Pam Fitzgerald, left, with her mother.

Midtelephone conversation, Pam Fitzgerald pauses. Her dog's barking at the FedEx truck. "Oh, it's my medicine being delivered," she says matter-of-factly. Daily medicine keeps her moving forward, for now.

For the past 3.5 years, the 49-year-old Northern Virginia resident has been battling metastatic metaplastic breast cancer, a rare and aggressive form of the disease that, in her case, initially presented as redness and skin irritation rather than a lump in the breast.

When Pam was diagnosed, she also learned, via genetic testing, that she has the BRCA1 mutation, an inherited gene mutation that predisposes the carrier to a higher risk of developing breast and ovarian cancers. While this information presents a burden to patients, who now realize their family members may also share this genetic predisposition to cancer, it's also beneficial.

The ability of experienced clinician-scientists to glean information about a patient's genetic makeup and, subsequently, evaluate the potential benefit of targeted, experimental therapies is especially important in complex cases like Pam's, in which standard radiation, chemotherapy and surgery are not enough to keep the disease in check.

The promise of this type of individualized care, known as "precision medicine," has proven a bright spot on Pam's turbulent cancer journey, during which she's had to cope with her own overwhelming and ever-shifting medical circumstances, but also those of others who are near and dear to her.

A world suddenly turned upside down

Pam's personal foray into the seemingly relentless world of cancer began on Thanksgiving Day in 2013, when she and her mother were volunteering at a local "turkey trot" foot race. At the event, her mother, who Pam describes as her best friend, suffered a seizure. That led to a stint in the hospital, where she was diagnosed with stage 4 lung cancer.

"The wheels came off, and we were free falling," says Pam, a single marketing consultant who quickly became her mother's strongest advocate and caregiver. About six months later, Pam was diagnosed with metaplastic breast cancer. It was May 4, 2014—the day before the festive holiday known as Cinco de Mayo.

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Here I Am

One Patient's Inspirational Approach to Living with Metastatic Breast Cancer

Barbara Mohler has been fighting breast cancer for 37 years. First diagnosed in 1980, she has battled many recurrences. "For a long time, I felt like I was just one of many," she says. Unsatisfied with that feeling, in 2002, she placed a call to Johns Hopkins, hoping to find a different path for her care.

"They said there was a new oncologist I could get an appointment with—Dr. Stearns—and she and I have been together ever since," Mohler says, laughing. "I tell Dr. Stearns that when she gets a new office, I want my name on the door too. I got her this far!"

Barbara Mohler and family

Vered Stearns is director of the Kimmel Cancer Center's Breast Cancer Program and she has treated Mohler's metastatic breast cancer for 15 years. Mohler, who describes herself as "picky," says the long relationship is indicative of her trust in Stearns. "If I feel that a doctor is not the doctor for me, I won't go back," she says.

At the Kimmel Cancer Center, Mohler says, she has been able to find doctors and nurses who have worked with her over the years to treat her as an individual and work with her to find the treatment plan that works best for her. "No two cancers are the same. I'm not the same as the person next to me with metastatic breast cancer," she says. "Dr. Stearns, her nurse Maureen Berg and everyone involved in my treatment at the Kimmel Cancer Center have recognized that, and that's important. It's made all the difference."

The 79-year-old has undergone a lumpectomy, a mastectomy, radiation and several types of chemotherapy since August 1980, when a doctor told her she had a few months to live. "I told that doctor I couldn't die because I had people depending on me."

Mohler is the mother of six boys—her oldest son was a freshman in high school and her youngest was in first grade when she was first diagnosed. "The kids knew what I had, but we didn't make it anything sad," she says. "I believe that when you have cancer, you need to find the most positive reaction to everything you have to deal with. I wasn't going to give in to anything. I was going to fight and do what I had to do."

Mohler has lived in the small, close-knit town of La Plata, Maryland, for almost 50 years. "Everyone here knows my attitude," she says. Throughout her life she has looked for ways to share her positive approach, including her time as a junior high teacher. Her cancer treatments have spanned most of her career, and this meant there were times she had to improvise and make alternative lesson plans. When she wasn't feeling well, her students pitched in. "And we all learned something. I would always ask them, 'What will we do that's fun today?' And then say, 'Whatever we'll do, we're going to laugh.'"

During her treatment, she has volunteered in hospice and in a La Plata cancer group that visits cancer patients referred from local hospitals and doctors' offices. Mohler carries her positive outlook into these visits. "I just like to talk to people, ask them what they're going through, ask them about their treatment. I wanted them to know that I understood what they were going through and encourage them. I'd tell them, 'If I can do it, you can do it.'"

Mohler says she is grateful for the help she and her husband, Ed, who is legally blind, receive from their sons and grandchildren who live nearby. Her granddaughter and other family members take Barbara and Ed to doctors' appointments—including trips to Baltimore for her appointments with Stearns. When Mohler needed injections to prevent blood clots during a recent treatment, her oldest son came daily to give her the shots, and a longtime family friend who Mohler calls her "daughter" often flies in from Florida to help with driving and housework.

"It has been difficult to depend on them, but they have been wonderful," Mohler says. "And my husband does so much, he has been wonderful, and he helps keep the house immaculate."

Until recently, when her instructor moved away, Mohler was attending a yoga class three times a week, "and I loved every bit of it," she says. "I need to find something else like that. I also love outside work, and I planted some flowers this spring, but I just don't always have the energy for it."

She also keeps in touch with a group of sorority sisters, some of whom she has known since grade school. They meet once a month, usually at Mohler's house, to say the rosary. They have also traveled together. "We have the best time. We act like kids ourselves. Sometimes we embarrass our own kids," Mohler says. "But life is to be enjoyed."

This spirit, and what she considers the best cancer care anywhere, has carried her through this lengthy battle with breast cancer. Barbara and Ed recently celebrated their 60th wedding anniversary, surrounded by their family and friends.

"I want people to know you can live with cancer," says Mohler. "Look at me. I've been fighting breast cancer for almost half of my life, but here I am."

New App Helps Breast Cancer Patients *Thrive*

Breast cancer patients receive a lot of information, and it can be overwhelming. Breast Cancer Program Director **Vered Stearns** says that was the inspiration for a new patient app, funded by Under Armour, that puts just about anything breast cancer patients need or want to know in the palm of their hands.

With a smartphone, patients will soon be able to download the secure and password-protected mobile application called *Thrive* that guides and educates breast cancer patients throughout diagnosis, treatment and beyond.

Patients will no longer need to rely on memory or quickly written notes they jot down during their appointments. Now, there is an app for that.

Thrive provides a detailed list of appointments, including how to get to Johns Hopkins; detailed information on the diagnosis, including type of breast cancer, stage of cancer, size of tumor, hormone status, HER2 status, genetic factors (such as BRCA negative or positive) and goals of therapy; and a detailed description of therapy, including all of the drugs a patient will receive and how long they will take each one. There is a place to enter notes about topics patients want to ask the doctor or nurse. The app also has a "learn" section that addresses common concerns and defines all of the medical jargon.

The app developers involved breast cancer patients, doctors, nurses and patient navigators throughout the design process and prototype testing. The only thing a breast cancer patient won't find in this app is pink. When patients were surveyed, they requested any color but pink, opting instead for a calming green. The patients also chose the app's name.

Thrive was developed by emocha Mobile Health and is expected to be available to patients in six to 12 months. ■

Saraswati Sukumar, Ph.D., left, and visiting scientist Guannan Wang, M.D.

Blood Test Predicts Breast Cancer Survival

Breast cancer researchers **Sara Sukumar, Ph.D.**, and **Mary Jo Fackler, Ph.D.**, developed a blood test that identifies breast cancers at greatest risk of recurrence. The test, called cMethDNA, finds cancer DNA in the blood and a chemical alteration to the DNA, known as hypermethylation, that promotes unchecked cancer cell growth and predicts an aggressive cancer. The test was studied in women with advanced breast cancer, and patients who had higher levels of hypermethylated DNA had shorter periods of progression-free survival. Additional research, led by **Antonio Wolff, M.D.**, will explore the test as a way to predict, early on, if a cancer is responding to therapy. "There's a great need in cancer patients to be able to quickly and easily assess if a particular treatment is working to be to able switch to another if it's not, and avoid potential side effects and cost," says **Kala Visvanathan, M.B.B.S., M.H.S.**, a co-author on the study.

New Immunotherapy Drug

In an early clinical trial, a new drug called CPI-444 appears to keep cancer in check, alone and in combination with another immunotherapy. The drug targets the adenosine pathway, which acts as an on/off switch for cancer-attacking immune T cells. The trial has 11 participating hospitals, and cancer immunology expert **Leisha Emens, M.D., Ph.D.** is leading the study at the Kimmel Cancer Center. "Some patients receiving either CPI-444 alone or in combination with atezolizumab are experiencing control of tumor growth," says Emens. The drug is being tested in triple-negative breast cancer, lung cancer, kidney cancer, melanoma and other cancers.

"SOME PATIENTS RECEIVING EITHER CPI-444 ALONE OR IN COMBINATION WITH ATEZOLIZUMAB ARE EXPERIENCING CONTROL OF TUMOR GROWTH."

– LEISHA EMENS

Healing the Healers

Every month, breast cancer physicians, nurses and other staff gather for a lunch that has become a time to reflect and heal, in acknowledgment of patients lost and the challenging and stressful jobs they have.

Facilitated by **Rab Razaak**, Director of Outpatient Palliative Medicine at Johns Hopkins Medicine, the lunch group discusses the grief and anxiety—as well as the positive, supportive events—they experience in their work. The lunch meetings often begin with the prompt of a poem or a relevant video and offer relaxation techniques, such as guided meditation. They are held the first Wednesday of every month.

"We've found it to be a great way to develop a supportive, family-type environment during the work day," said Razaak, who was invited by Breast Cancer Program Co-Director **Vered Stearns** to start the lunches. "It's a focused time to reflect and share our feelings. To have this come from our leadership is really impressive. It shows how invested Dr. Stearns is in her team."

"It is an opportunity for us to come together to relax, discuss emotionally challenging cases, but more importantly, focus on the good and the positive of what we do every day. I always leave these meetings feeling less stressed, renewed and better prepared to care for our patients," says nurse practitioner **Carol Riley**.

Navigating Breast Cancer


Jill Mull and Elizabeth Saylor

Young women facing a breast cancer diagnosis and treatment often find it challenging to juggle treatment with caring for their family, the demands of their job and other pressures of day-to-day life. Enter the patient navigator. Patient navigators **Jill Mull, M.Ed.**, and **Elizabeth Saylor, M.S.W.**—both cancer survivors—work primarily with breast cancer patients ages 45 and younger as part of Johns Hopkins LiveWell Center, helping women balance their priorities, get connected to resources and overcome barriers to care. They collaborate with a patient's breast cancer team to give women the best experience during a difficult time.

Q: How do patient navigators help women?

MULL: A lot of young women who are going through a diagnosis of breast cancer have very specific needs that can't all be met during their medical appointment. For example, they may need some help overcoming barriers to care or wish to be connected to resources. We spend time informing them about what is available to them and helping guide them through their cancer journey.

SAYLOR: We work together with young women to address some of the competing priorities that they have in their lives in addition to their cancer. There's never an "ideal time" to have cancer, but in young adulthood—your 20s, 30s and 40s—there are many things that women are investing their energy and emotion in, like having a family, starting a new job, or going to college or graduate school. Cancer comes at a time in their lives when they are developing new relationships and solidifying their identities as working professionals, mothers and wives/partners.

READ MORE: http://bit.ly/KimmelCancerPubs *Look for Breast Matters*

Ben Park, M.D., Ph.D., was named associate dean for postdoctoral affairs for the school of medicine.

The Baltimore Orioles' Birdland Community Heroes Program honored breast cancer prevention expert **Kala Visvanathan, M.B.B.S.** The program acknowledges community heroes who inspire through their spirited commitment to extend a hand in charity, service, hope and harmony.

The Dr. Susan Love Research Foundation presented **Saraswati Sukumar, Ph.D.**, with its International Symposium on the Breast Collaborator Award for enthusiastic support and decades of partnership with the foundation.

Elissa Bantug received the Morgan Pressel Foundation Fifth Annual Kathryn Krickstein Pressel Award. Morgan Pressel Bush called Bantug "maybe the most deserving recipient we've ever had," recognizing Bantug's personal battle with breast cancer and her impressive survivorship work, taking her own experiences and helping others battling the disease.

Antonio Wolff, M.D., was included on Thomson Reuters' 2017 list of the most highly cited researchers in the sciences and social sciences in the world. Wolff was also named one of the American Society of Clinical Oncology's Advocacy Champions for educating lawmakers on important cancer policies that help ensure high-quality cancer care in the U.S. remains available to all.

Breast Matters won a Spring 2017 Digital Health Award. The award honors high-quality digital health resources for consumers and health professionals.

Prevention Means Hope

Brenda Cho was a working mother of a 2-year-old and 4-year-old when she received a diagnosis of stage 4 metastatic breast cancer in March 2015. It was her first diagnosis—she had never been diagnosed with early-stage cancer, and she had no family history of breast cancer. She had just turned 37 years old.

Cho met her oncologist, **John Fetting**, on the day of her diagnosis. "I still remember how he made the effort to call me that evening after speaking with some colleagues about the treatments we would pursue," she recalls. "I thought that's what all oncologists did, but he really went above and beyond on what was one of the most difficult days of my life."

Cho is a strong supporter of the John Fetting Fund for Breast Cancer Prevention at Johns Hopkins. The fund supports breast cancer prevention research, from developing new ways to predict an individual's risk for cancer from breast tissue analysis to testing novel drugs and natural compounds to prevent breast cancer.

As a metastatic cancer patient, Cho says, "It may not make a lot of sense to people that I am championing prevention. I'd love to find a cure, obviously, but I'm also focused on meaningful treatment to prevent people from getting a breast cancer diagnosis. This is very important to me as a mother and a sister." Cho says she has three sisters who are all at increased risk of developing breast cancer.

"The Fetting Fund can help identify steps one can take so that future generations at increased risk for breast cancer never have to wonder every day, 'When is it coming?'" Cho says.

She finds ongoing support with a monthly Johns Hopkins Breast Center group for young metastatic breast cancer patients, one of the few in the country for patients under age 45.

In June 2017, after two years of remaining stable, her breast cancer began to progress again. She is participating in a clinical trial of a promising new treatment. "I'm enthusiastic about medical research," Cho says. "I think the word 'trial' can scare people because it sounds too risky or experimental," she says. "To me, the underlying question about whether a new treatment is effective for metastatic breast cancer patients was appealing. We're not going to find out what works unless patients help doctors explore these new therapies. There's really no new drug that gets approved without this kind of extensive testing. We need more research for better treatments, as well as ongoing research on prevention, to improve outcomes for patients and their families at risk."

At a 2016 Fetting Fund event, Cho shared the details of her diagnosis and treatment with a public audience for the first time. "Everyone was listening to my story, and I was so touched because it can be a challenge to share a grim diagnosis openly. But what I want those who hear my story or others battling breast cancer to think is, 'What can I do to get involved? How can I help to change the course of breast cancer?'" For Cho, the Fetting Fund provides that opportunity, so she spoke again to potential Fetting Fund supporters at a September 2017 event.

"I want to educate people, to break down the barriers and for people to gain a better understanding of what it means to live with metastatic disease." ■

Survivor Soul Stroll

SATURDAY, MAY 13, 2017, marked the first annual Survivor Soul Stroll to raise money and awareness for breast cancer research. Radio One and its affiliate stations were lead sponsors of Soul Stroll, held at the Canton Waterfront Park, and the Johns Hopkins Kimmel Cancer Center was a co-sponsor. Breast cancer prevention expert **Kala Visvanathan** and **Dina Lansey,** who heads Cancer Center efforts to increase minority participation in clinical trials, spoke about their work to a crowd of more than 500 people.

Geraldine Walton, a 72-year-old breast cancer survivor and Kimmel Cancer Center patient, was among the participants, walking 2.5 miles in memory of her sister, who died of breast cancer 10 years ago. Despite a hip replacement and knee problems, breast cancer surgery just 10 months before the event, and rainy weather, Walton donned pink and white bow earrings and a ring that she bought just for the day and joined the other walkers. "People were cheering me on," says Walton. "It felt so good knowing we were raising money and awareness for breast cancer."

From left, Kala Visvanathan, M.B.B.S. and Dina Lansey, M.S.

THE JOHN fettingfund FOR BREAST CANCER PREVENTION

Update on Fetting Fund Supported Research

Curcumin Spice: **Saraswati Sukumar, Ph.D.**, is working on the creation of a novel, simple and safe design for long-term oral administration of the spice curcumin for prevention of breast cancer in women. Curcumin is used in Indian medicine as a treatment for cancer and dates back hundreds of years. Intense studies in the last 25 years have resulted in the demonstration of its cancer-preventive activity in laboratory animals. Tumor regression was shown to occur through suppression of inflammation and other key mechanisms in many types of cancer models, including breast cancer.

New Test: **Ben Park, M.D., Ph.D.**, and his team are developing a test to detect breast cancer at its earliest stages in women who carry BRCA1 or 2 gene mutations. Women with BRCA1 or 2 gene mutations often undergo active surveillance and/or prophylactic surgeries to mitigate this risk and improve outcomes. However, for active surveillance, screening by mammography and/or breast MRI scan can lead to false-negative and false-positive results. Park's blood test measures cancer mutations in blood plasma and may serve as an additional screening tool for BRCA carriers undergoing active surveillance.

Honokiol: The root and stem bark of the magnolia species have been used for centuries in traditional Asian medicine to treat anxiety, nervous disorders, fever, gastrointestinal symptoms and stroke. The therapeutic benefits of the magnolia species have been attributed to honokiol, a natural phenolic compound isolated from an extract of seed cones from magnolia tree bark. The laboratory of **Dipali Sharma, Ph.D.**, recently showed that honokiol prevents growth, invasion and migration of breast cancer cells, and that honokiol treatment significantly reduces tumor growth in laboratory models of breast cancer. She is examining the chemopreventive potential of honokiol using mouse models of spontaneous tumor development.

Prediction Tool: **Kala Visvanathan, M.B.B.S.**, and her team are investigating whether DNA changes, such as methylation (when healthy gene expression changes to a disease pattern), and mutations in normal breast tissue are indicators of future breast cancer risk. The research team is comparing DNA alterations in tumor tissue with unaffected breast tissue from within the same breast and the opposite breast. This information will help determine whether assessing methylation in breast tissue is a promising tool to predict cancer risk and therefore warrants further study.

LEARN MORE: http://bit.ly/fettingfund

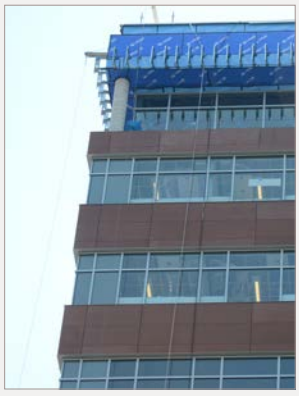
Swim Across America

Adoptive T cell therapy is a type of immunotherapy that relies on identifying killer T cells that react to mutant proteins from a patient's own tumor. Unfortunately, the mutant proteins that have been targeted in this way are not shared among tumors from different individuals, making this approach difficult to apply widely in the clinic. Now, researchers have identified a mutant tumor antigen, called GATA3, that is common among 5 to 7 percent of all breast cancer patients—about 10,000 to 15,000 women and men each year in the United States alone. **Josh Lauring** received a Swim Across America grant to test T cells from healthy donors for their ability to specifically recognize and destroy breast cancer cells with GATA3 mutant proteins. This proof-of-principle could lead to new immunotherapy treatments for hormone receptor-positive breast cancer.

Marcie and Ellen Foundation

The Marcie and Ellen Foundation, in memory of Marcie Westermeyer and Ellen Ervin, donates all of its proceeds from an annual benefit dinner to support the research of the Kimmel Cancer Center Breast Cancer Program. Currently in its fifth year, the foundation is supporting the liquid biopsy research of **Ben Park, M.D., Ph.D.**

Liquid biopsy uses tumor plasma DNA to measure microscopic breast cancer cells remaining after surgery and other therapies to distinguish patients who are cured, and could avoid additional treatment, from those who still have tumor cells remaining and will need more therapy.



Skip Viragh Outpatient Cancer Building

The Skip Viragh Outpatient Cancer Building is nearing completion, with a planned opening in late 2018. The diagnostic and treatment facility includes the Under Armour Breast Health Innovation Center.

JOHNS HOPKINS
BREAST MATTERS

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at Johns Hopkins Office of Public Affairs

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Each contribution to the Breast Cancer Program at the Johns Hopkins Kimmel Cancer Center makes a difference in the lives of cancer patients here at Johns Hopkins and around the world.

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